REMARKS

This Amendment is respectfully submitted in response to the Final Rejection mailed December 15, 2008. It is timely filed in view of the three-month period for response set therein. A Request for Continued Examination is respectfully submitted concurrently herewith. Reexamination and reconsideration of the rejections set forth therein in light of the following remarks are courteously requested.

Claims 73-86 are pending in the above-identified patent application.

The Final Rejection of December 15, 2008 again rejected claims 73-78 under 35 U.S.C. §103(a) as being unpatentable over Meybeck et al., US 5,034,228 in view of Sessa et al. JAOCS vol. 69(3) 1992, 209-212 ("Sessa et al.") and Seiberg et al. J. Invest. Dermatol. 109:370-376 1997 ("Seiberg et al."). The basis for maintaining this rejection was stated as follows:

> The affidavit under 37 CRF 1.132 filed on 9/12/08 is insufficient to overcome the rejection of claims 73-86 based upon the 103(a) rejection as set forth in the last Office action because: All that is required of the claims is to have a non-denatured soy extract (see claim 73 for example). In contrast, denatured, as understood by one of ordinary skill in the art is a structural change in a molecule. Meybeck teaches a product of soy extract-soya lecithin, tretinoin and a solvent which is not an alcohol. Therefore, denaturation of the lecithin would not occur.
>
> *In arguendo*, even if the solvent is found to denature the extract, the "active agent-trypsin" will still be present in the soya lecithin whether denatured or non-denatured. Therefore it would be expected that trypsin (the active agent) would react with tretinoin to give the same result of treating acne, as claimed (see claim 73 for example). [Final Rejection, pp. 2-3]

The Final Rejection further stated that:

> …With regard to the Meybeck et al.…discloses a suspension of soya lecithin, 0.1 g tretinoin (see col. 3, lines 60-65). Accordingly, the limitation set forth in claim 73 is therefore met. As to the limitation of non-denatured soybean extract, soya lecithin is considered as a non-denatured extract of soybean (giving its broadest claim interpretation – the extract product should be non-denatured regardless of how it is obtained). Meybeck do not teach that the soy lecithin is defatted, which is considered a denatured soy lecithin. All the claims required is a non-denatured soybean extract having a trypsin inhibiting activity. Meybeck, as indicated by Applicant, states clearly the formulation is employed for the treatment of acne, the claims recite a method of treating acne, and therefore the limitations as set forth in the claims are met by the teaching of Meybeck.
>
> The introduction of Sessa shows that, and also admitted by applicant, that there is trypsin in soybean flour. Seiberg as introduced for its teaching that acne is eliminated by trypsin treatment. Therefore, the combined knowledge of the cited prior art would have led one of ordinary skill in the art the art to formulate of formulation comprising a tretinoin from a non-denatured soybean extract that is employed for the treatment of acne. [Final Rejection, p. 4]

Applicants respectfully request reconsideration of the rejection of claims 73-38 under 35 U.S.C. §103(a) in view of the ensuing discussion.

Applicants respectfully request reconsideration of the foregoing rejection in view of the ensuing remarks and Declaration of Connie Baozhen Lin, Ph.D. respectfully submitted concurrently herewith ("Lin Declaration").

The Meybeck et al. patent relates to "hydrous lipidic lamellar phases or liposomes containing, as an active agent, a retinoid or a structural analogue of retinoid…These compositions are more efficient against acne and less irritant for the skin…" [Meybeck, et al., Abstract]. "Hydrogenated soya lecithin" [Meybeck, et al., col. 8, l. 2] is mentioned as one of the components of a composition for treating acne skin. However, applicants respectfully assert that Meybeck et al. neither suggests nor describes the compositions or methods of applicants' invention.

Meybeck et al. utilizes lecithin in the liposomes described therein ***as a delivery vehicle***, to form the lipidic layer portion of the liposomes. Lecithin, according to Meybeck et al., ***is not used as an active agent for treating acne***. Soybeans have a multitude of components, including lecithin, which can be separated out from the natural beans in several ways. As stated in applicants' previous response, lecithin is removed from the soybeans using organic solvents—these solvents solubilize the lipidic lecithin molecules and separate them from the remainder of the beans. However, as demonstrated by the results set forth in the Lin Declaration submitted concurrently herewith, soy lecithin does *not* contain trypsin inhibitory activity.

The Lin Declaration demonstrates that commercially available soy lecithin, even at a level over four times the amount present in non-denatured soy made in accordance with the methods set forth in the above-captioned patent application, ***does not contain trypsin inhibiting activity***. [Lin Declaration, ¶¶4, 5]. The component of soybeans that is known in the art as "lecithin" is the chemical "phosphatidylcholine" [Lin Declaration, Exhibit 2, Liu, et al., p. 32]. This was the chemical that was tested in conjunction with the Lin Declaration. As set forth above and in the Lin Declaration, this material does not contain trypsin inhibitory activity. Thus, the teachings of Meybeck et al. would not have led one of ordinary skill in the art to the compositions and methods of applicants' invention.

Furthermore, applicants respectfully draw the attention of the Patent Office to the description set forth in Claim 73. Claim 73 requires the presence of a " nondenatured soybean

extract ***having trypsin-inhibiting activity***". [Claim 73, emphasis added] This description clearly relates to soybean-derived extracts that contain such activity, ***not*** to extracts that do ***not*** contain such activity.

Sessa et al. relates to the determination that trypsin inhibitor activity is present in toasted soybean flour. [Sessa et al., p. 784]. Sessa et al. does not remedy the inadequacies of Meybeck et al. in suggesting the compositions and/or methods of applicants' invention to one of ordinary skill in the art at the time of the invention. Nowhere does Sessa et al. indicate that trypsin inhibitor activity is useful in treating skin conditions. Rather, Sessa et al. merely indicates that there is trypsin inhibitor activity in soybean flour. In fact, Sessa et al. states that trypsin inhibitor activity may be related to negative physical effects in rats fed with toasted soybean flour and that ***its presence should be eliminated***:

> Since long term rat feeding studies with raw, toasted and overtoasted soybean flour treatments show a linear dose relationship for pancreatic lesion formation (1), our results are consistent with the hypothesis that attributes hyperplasia and tumor formation to the proteinaceous TI's [trypsin inhibitors]. ***Methods will be developed to inactivate the protease inhibitors, both in the purified state and in food systems.*** [Sessa et al., pp. 787-788] (emphasis added)

Thus, applicants respectfully submit that Sessa et al. would teach away from utilizing soybean extracts containing trypsin inhibitors.

Nor would the Seiberg et al. publication, taken alone or in combination with Meybeck et al. or Sessa et al. have lead one of ordinary skill in the art to the compositions and/or methods of applicants' invention. In fact, applicants respectfully submit that it would have lead ***away*** from their invention.

The Seiberg et al. publication relates to the use of ***trypsin*** (as opposed to ***trypsin inhibitors***) in inducing desquamation and utriculi-epidermal differentiation in skin:

> The pathogenesis of acne vulgaris is multifactorial, resulting from excessive follicular keratinization and sebum production and bacterial proliferation contributing to inflammation. Effective management should be directed to the combination of these four factors. While topical retinoids are considered to be the most effective single comedolytic agent, their clinical efficacy is limited by their irritant effects. Here we show that ***the combination of tyrpsin with suboptimal doses of tRA could lead to a potentially effective comedolytic agent with a lower irritation profile***. [Seiberg, et al., p. 375]. (emphasis added)

Applicants respectfully submit, in view of the foregoing, that Seiberg et al. teaches away from the compositions and methods of applicants' invention. Rather than suggesting that *trans* retinoic acid be combined with ***trypsin inhibitor*** to treat acne, Seiberg et al. clearly suggests that tRA be combined with ***trypsin*** to treat acne.

Therefore, if one of ordinary skill in the art were to have read Meybeck et al., Sessa et al. and Seiberg et al. together, applicants respectfully assert that that person would not have been lead to the compositions or methods of applicants' invention. Meybeck et al. mentions a lipidic extract of soy that would most likely ***not*** contain trypsin inhibiting activity which, indeed, has been demonstrated in the Lin Declaration; Sessa et al. merely states that soy may contain trypsin inhibitory activity, but that it is ***undesirable***; and Seiberg et al. suggests that trypsin, ***not trypsin inhibitor***, would be combinable with a retinoid to treat acne. This would have lead to the opposite result than that of the compositions and methods of applicants' invention. In view of the foregoing discussion, applicants respectfully request reconsideration of the rejection of claims 73-78 under 35 U.S.C. §103(a).

In view of the foregoing discussion, applicants respectfully request reconsideration of the rejection of claims 73-78 under 35 U.S.C. §103(a).

The Office Action of December 15, 2008 further rejected claims 79-86 under 35 U.S.C. §103(a) as being unpatentable over Meybeck et al., US 5,034,228 in view of Sessa et al. JAOCS vol. 69(3) 1992, 209-212 ("Sessa et al.") and Seiberg et al. J. Invest. Dermatol. 109:370-376 1997 ("Seiberg et al.") as applied to claims 73-78. The grounds for maintaining this rejection were given as follows:

> Meybeck teaches 2 g of soy lecithin and 0.1 g of tretinoin which examiner has interpreted to be within the claim invention of 79, 81-83 and 85-86…One of ordinary skill in the art would be motivated to optimize the concentration of the active agents for the treatment of acne because it is known in the art that topical application of the retinoids in the past gave undesirable effects such as irritation…Based on that the determination of a dosage having the optimum therapeutic index is well within the level of the ordinary skill in the art, and the artisan would be motivated to determine the optimum amounts to get the maximum effect of the drug, hence the reference makes obvious the instant invention. [Office Action, p. 5]

Applicants respectfully request reconsideration of the foregoing rejection in view of the ensuing discussion.

As set forth above, Meybeck does not teach or suggest the use of a soy extract containing soy trypsin inhibitory activity at any level of presence in a composition. Sessa et al. merely states that certain soybean materials can contain residual trypsin inhibitory activity, but that such activity is undesirable. Seiberg et al. suggests that ***trypsin***, rather than soy ***trypsin inhibiting*** proteins, would be useful in treating acne. These references, taken together or separately, would not have lead one of ordinary skill in the art to the compositions or methods of applicants' invention.

In view of the foregoing discussion, applicants respectfully request reconsideration of the rejection of claims 79-86 under 35 U.S.C. §103(a).

Accordingly, applicants respectfully submit that the above-captioned application is now in condition for allowance. Accordingly, favorable reconsideration of the above remarks and an early allowance are courteously solicited. If the Examiner has any comments or suggestions that could place this application in even better form, the Examiner is requested to telephone the undersigned Attorney at the below-listed number.

If there are any other fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 10-0750.

Respectfully submitted,

/Andrea L. Colby/

Andrea L. Colby
Reg. No. 30,194
Attorney for Applicants

Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-2792
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